

## Acute Infantile Haemorrhagic Oedema: Measles Vaccination as Possible Triggering Factor

Yasemin Saray<sup>1</sup>, Deniz Seçkin<sup>1</sup>, Evren Sarifakioğlu<sup>1</sup>, A. Tülin Güleç<sup>1</sup> and Beyhan Demirhan<sup>2</sup>

Departments of <sup>1</sup>Dermatology and <sup>2</sup>Pathology, Başkent University Faculty of Medicine, 12. Sokak, No. 716, Bahçelievler-06490 Ankara, Turkey. E-mail: yaseminsaray@hotmail.com

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Sir,

The entity now known as acute infantile haemorrhagic oedema (AIHO) of the skin was first described by Snow (1) in 1913. This disease primarily affects infants younger than 24 months of age, and is characterized by low-grade fever, sudden-onset purpura (often in a cockade pattern) and inflammatory oedema of the limbs and face. The most striking feature of AIHO is the contrast of these dramatic cutaneous signs in a patient who is otherwise in good general condition. In most cases of AIHO, the disease is confined to the skin with no visceral involvement. The course of the disease is short and benign, and patients show complete spontaneous recovery (2–6).

The aetiopathogenesis of AIHO is not well understood, but bacterial (3–5, 8) or viral infection (3, 4, 10), vaccination (3, 4) and drug intake (3, 4, 7–9) have all been proposed as causes. The authors of previous case reports agree that AIHO should be classified within the spectrum of leucocytoclastic vasculitis (3–9, 11, 12); however, the histopathological findings do not always meet the criteria for leucocytoclastic vasculitis (4). Here, we report an infant with AIHO that may have been triggered by measles vaccination. The histopathologic criteria for leucocytoclastic vasculitis were absent in this case. To our knowledge, this is the first report of AIHO occurring after measles vaccination.

### CASE REPORT

A 17-month-old male infant was hospitalized with fever and asymptomatic erythematous, edematous, ecchymotic lesions on the limbs and face that had been present for 2 days (Figs 1 and 2). The lesions had started as a few erythematous areas on the limbs. Over 2 days, they rapidly enlarged, changed to a purple colour, and spread to involve his face and all the surfaces of the limbs. Swelling also developed in his hands, feet and knees. Physical examination revealed extensive erythematous, polycyclic macules and plaques on the patient's face and limbs, inflammatory oedema and well-defined ecchymotic targetoid lesions on the dorsa of the hands, feet and knees. The infant was otherwise in good health except for a low-grade fever (38.5°C). His parents reported that he had received a measles vaccination approximately 3 weeks before the lesions first appeared. There was no history of medication or infection preceding the skin lesions.

A complete blood cell count revealed neutrophilic leucocytosis. Results of tests for liver and renal function, erythrocyte sedimentation rate, anti-streptolysin-O titre, urinalysis, fasting blood glucose level and levels of C-reactive protein, rheumatoid factor, C3 and C4 were all in the normal range. Antinuclear antibody and anti-DNA antibody investigations were negative. Throat, blood and urine cultures showed no growth. A 3-mm punch-biopsy specimen was obtained from a lesion on the leg. Histopathology showed a mild perivascular mixed infiltrate consisting of lymphocytes, neutrophils and eosinophils, as well



Fig. 1. Erythematous and annular plaques on the face. Note the oedema of face and upper limb.

as mild oedema and extravasated erythrocytes in the papillary dermis. No fibrinoid necrosis or nuclear dust was observed in the vessel walls. Direct immunofluorescence testing was negative for IgG, IgA, IgM, C3 and C1q deposition. Intravenous ceftriaxone was administered empirically for 3 days and hydroxyzine suspension was given for 5 days. Ceftriaxone was

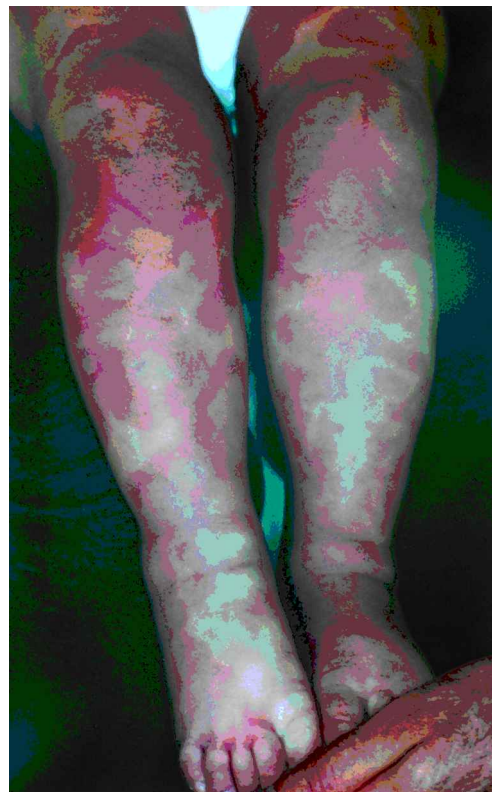


Fig. 2. Target-shaped ecchymotic lesions and oedema of the lower limb.

discontinued after the bacterial cultures were confirmed negative. The skin lesions resolved completely and the fever subsided within 5 days. The patient is currently well and has had no recurrence in 6 months.

## DISCUSSION

AIHO is not a frequently reported disease. Some authors (8, 11, 12) consider it to fall within the spectrum of Henoch-Schönlein purpura, whereas others (3–7, 9) believe it is a separate clinicopathologic entity and have proposed the term “acute benign cutaneous leucocytoclastic vasculitis of infancy” (3). The disease primarily affects infants between 4 months and 2 years of age. Its two main clinical features are purpuric-ecchymotic plaques (medallion-like or in a cockade pattern) and inflammatory oedema, both typically occurring on the face and limbs, and particularly the dorsa of the hands and feet (3–9). Our patient’s age, the typical clinical picture and the locations of the lesions all matched the classical description of AIHO (1–5). The most striking feature of AIHO is the contrast between the rather dramatic cutaneous skin lesions and the general well-being of the child, apart from a mild fever (3, 4). This was the situation in our case. Reports state that AIHO is mostly limited to the skin, with visceral involvement and systemic complaints being extremely rare (3–9). There were no systemic problems or visceral involvement in our patient.

The precise pathogenetic mechanisms behind AIHO are unknown. A history of preceding viral (3, 4, 10) or bacterial infection (3–5, 8) and/or drug intake (3, 4, 7–9) is present in the majority of reported cases. The most common causes suggested in the literature are various forms of infection (3–10). Upper (3–9) and lower respiratory tract infection (3, 4), neck abscess (4) and urinary tract infection (4, 5) have all been noted before or in association with AIHO. Most previously reported patients with AIHO have had upper respiratory infection (3–9). Viral illnesses such as measles (4), varicella (5) and adenovirus infection (10) have also been found to precede the onset of AIHO. However, in addition to their infections, almost all of these patients had a history of single- or multiple-drug intake, most commonly antibiotics and anti-inflammatories (3, 4, 7–9). As a result, it has not been possible to claim a definitive association between infection or drug intake and AIHO.

To the best of our knowledge, only two cases of AIHO occurring after vaccination have been documented in the English literature (3, 4). In one instance, AIHO developed 2 days after diphtheria-pertussis-tetanus and polio vaccination. This patient also had concomitant respiratory and urinary tract infections, so the underlying cause of AIHO was not clear (3). In the other case, the disease appeared 2 weeks after diphtheria-pertussis-tetanus vaccination (4). Our patient received a measles vaccination 3 weeks before his first AIHO lesions appeared. The absence of other possible aetiological factors suggests that the measles vaccination, acting as an antigenic stimulus, may have triggered the condition. AIHO is a benign entity, and cases resolve spontaneously and completely; however, it is important that all putative triggering factors be investigated so that the aetiopathogenesis of this peculiar disease can be defined.

The histopathologic features of AIHO also deserve to be

mentioned. The findings vary from typical leucocytoclastic vasculitis (3, 6–9, 11, 12), with or without fibrinoid necrosis, to less specific findings of a lymphohistiocytic perivascular infiltrate with erythrocyte extravasation (4). However, histopathological examination was not performed in all the previously reported cases (3, 4). Although true vasculitis was not observed (4) or clearly defined (4, 5) in some of the patients, the authors unanimously consider AIHO to be a form of leucocytoclastic vasculitis (3–9, 11, 12). Moreover, some of them (8, 11, 12) regard the condition as a variant of Henoch-Schönlein purpura because of overlapping features in the clinical and histopathological pictures. However, the histopathological diagnosis of leucocytoclastic vasculitis requires that one of two major criteria are met, namely, the presence of fibrinoid necrosis or leucocytoclasia (13). It seems likely that in some reported cases of AIHO (4), histopathological naming of leucocytoclastic vasculitis may have been incorrect. We observed neither of the main histopathological features of leucocytoclastic vasculitis in our patient, who had obvious clinical characteristics of AIHO. We propose that AIHO should be considered a distinct clinical entity that may or may not be associated with leucocytoclastic vasculitis.

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